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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/375,609	08/17/1999	LAWRENCE A. RHEINS	DERM1100-1	5338

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EXAMINER

SPECTOR, LORRAINE

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/375,609

Applicant(s)

RHEINS ET AL.

Examiner

Lorraine Spector, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-65, 71, 72, 76-78, 80-83, 85-87, 149-161, 163 and 164 is/are pending in the application.
- 4a) Of the above claim(s) 11-63 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 64, 65, 71, 72, 76-78, 80-83, 85-87, 149-161, 163 and 164 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 11-65, 71-72, 76-78, 80-83, 85-87, 149-161 and 163-164 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 09152003 6) ☐ Other: _____

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DETAILED ACTION

Claims 11-65, 71-72, 76-78, 80-83, 85-87, 149-161 and 163-164 are pending.

Claims 64, 65, 71-72, 76-78, 80-83, 85-87, 149-161 and 163-164 are under consideration.

The rejection of claims 65, 149-156 and 161 under 35 U.S.C. §112, second paragraph is withdrawn in view of applicants arguments and amendments to the claims.

The rejection of claims 71, 156, and 159 under 35 U.S.C. §112, first paragraph for introduction of new matter is withdrawn in view of applicants arguments.

The rejection of claim 82 under 35 U.S.C. §112, first paragraph is withdrawn in view of applicants arguments.

The declaration by Dr. Nicholas Benson under 37 CFR 1.132 filed 9/15/2003 is insufficient to overcome the rejection of claims based upon Garofano et al. as set forth in the last Office action because:

(1) The tapes used in the Experiments described by Dr. Benson cannot be compared with those of Garofano et al., having been from different manufactures. Further, the tapes appear to have been selected for strength of adhesive, as Garofano et al. used CometTM strapping tape, whereas Dr. Benson's declaration states that "Scotch (3M) brand Packaging Tape Super Strength and (the second was) Scotch brand Strapping Tape" were used; it cannot be determined whether the adhesives used by the two brands are comparable, and the use of a "super strength" tape implies a greater adhesive strength. Similarly, different brands of stubs were used. Further, as the Garofano reference was published in 1996, adhesive strengths have increased widely in the art during the elapsed time period. Therefore, it cannot be determined whether or not the experiments conducted by applicant are comparable to those of Garofano et al. Finally, with respect to the data obtained by those experiments, it is noted that the number of strippings required is quite variable, ranging from a low of 12 to ≥ 25 . Given the variability, it seems clear that it cannot be concluded that the recitation that the skin is stripped 1-12 or a maximum of 25 times would render the claims patentably distinct from the disclosure of Garofano et al.

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The declaration by Dr. Gerald Krueger under 37 CFR 1.132 filed 9/15/2003 is insufficient to overcome the rejection of claims based upon Garofano et al. in view of Paludan et al. as set forth in the last Office action because:

At paragraph 10, Dr. Krueger states that there would not have been an expectation of success because skin is a rich source of RNAases. This argument has been fully considered but is not deemed persuasive because it appears to be opinion, and is not substantiated by fact or evidence. Further, it is well known in the art that *all* work involving RNA is difficult, because *all* tissues and cells are rich in RNAases. It is a normal part of protein metabolism that mRNA is made by a cell and then degraded by RNAases. All cells possess them. There is no reason for the person of ordinary skill in the art to have expected skin cells obtained by tape stripping to be inordinately different in this respect.

At paragraphs 11-12 declarant argues that the samples obtained by tape stripping would be too small to measure, and thus to amplify. This argument has been fully considered but is not deemed persuasive because once again this is opinion and is not supported by fact or evidence, and further, the Examiner finds that Paludan did not consider measurability to be indicative of an expectation of success (see response to arguments of the rejection, below).

Declarant's statement of the lack of other references disclosing the claimed invention is not pertinent to the grounds of rejection.

Declarant's argument with respect to the lack of control data in Garofano's results is not pertinent. There is no limitation regarding such in the claims. Further, as Garofano's results were published in a scientific publication, one must assume that they stood up to editorial review, and as such must have included controls, even if such were not considered worthy of mention. Regardless of such, the argument pertaining to contamination is mere conjecture, and is not supported by fact or evidence.

Declarant's surprise at the invention is mere opinion, and is not probative of patentability without further support as to why the person of ordinary skill in the art would not have expected success at modifying the teachings of Garofano et al. in view of Paludan et al.

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Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 160 is rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

Claim 160 is drawn to a method in which sodium lauryl sulfate is applied to the skin prior to taping and analyzing nucleic acids in the skin. It is noted that applicants have pointed out that the specification discloses an experiment in which such was done at pages 16-17. However, such is merely an experiment to determine the operability of the claimed method. The specification has no disclosure of why one would desire to perform the method of claim 160. In the absence of a disclosure of specific, substantial and credible utility, the Examiner concludes that the only use of the claimed method is for further research, either into the operability of the claimed method, or alternatively to determine the effects of SLS on gene expression in the skin. Neither constitutes a real world, readily available use. Accordingly, the claimed invention lacks utility.

Claim Rejections - 35 USC § 102 and §103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

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evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 64, 65, 76, 85, 86, and 161 remain rejected under 35 U.S.C. 102(b) as anticipated, and Claim 70 is rejected under(b) as anticipated by or in the alternative under 35 U.S.C. 103(a) as obvious over Garofano et al., Adv. Forensic Haemogenet 6:281-283, 1996.

Applicants traversal in the paper filed 9/15/2003 has been fully considered but is not deemed persuasive. The Benson declaration has been fully considered above, and is not persuasive in overcoming the rejection. With respect to applicants argument in which it is argued that the rejection neither anticipates each and every element of the claims and that there is no Graham v. Deere analysis of obviousness, this argument has been fully considered but is not deemed persuasive, as it fails to take account of the case law under which authority the rejection is made, *In re Best* 195 USPQ 430, 433 (CCPA 1977). It remains that Garofano et al. appears to meet the limitations of the rejected claims, or not to be patentably distinct from such, and applicants have not met the burden of overcoming this *prima facie* finding.

Applicants speculation at page 20 of the response regarding contamination has been fully considered but is not deemed persuasive, as (a) it is mere speculation and is not supported by facts or evidence, and (b) Applicants are arguing as though there were some limitation in the claims as to the success rate of the claimed methods, or alternatively some unexpected result, neither of which is the case. It remains that Garofano et al. disclose the analysis of genetic material that is stuck to tape in the form of skin cells, which is the method claimed here. Garofano et al. reasonably put into the hands of the public the claimed method, regardless of the number of tape strippings used, as it would have been routine experimentation in the art to determine the best or least possible number of strippings, and as Garofano et al. contemplate the use of the method in forensic applications in which the tape would only have been stripped a single time. Although applicants seek to distinguish their invention from the prior art on the basis of repetitions of stripping, there is no disclosure in the specification or claims of criticality

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of the number of times or manner in which the tape has stripped that would serve to go beyond the teachings of Garofano et al.

Claims 71-72 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Garofano et al., Adv. Forensic Haemogenet 6:281-283, 1996 for reasons of record in the previous Office Action.

Applicants arguments filed 9/15/03 have been fully considered but are not deemed persuasive. Applicants argument that there is no motivation nor reason to expect success at stripping 1-12 times based upon the disclosure of Garofano et al. This argument has been fully considered but is not deemed persuasive because as stated in the previous Office Action, the “skilled artisan would have been motivated to do so to minimize stress and trauma on the patient, both well-recognized motivations in the medical arts.” As for the reasonable expectation of success, Garofano et al. apparently thought there would be a reasonable expectation of success, as the introduction to the paper states: Adhesive tapes are often used in kidnapping cases or to wrap packages, and can represent important evidence related to crimes. For this reason, we investigated whether the cellular material stuck on different adhesive tapes could be employed for genetic analyses.” And the conclusion of the paper is: “we think the material stuck on the adhesive tapes can be considered an interesting source of DNA for investigation purposes.” Accordingly, it can be concluded that Garofano et al. contemplated, and considered the expectation of success reasonable at obtaining genetic material for analysis from tapes that had been used, e.g. on kidnapping victims, or by people wrapping packages, which would clearly have been “stripped” only one time. Accordingly, applicants argument is not persuasive.

Claims 77-78, 80-83, 149-154, 156-159 and 163-164 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garofano et al., Adv. Forensic Haemogenet 6:281-283, 1996, in view Paludan et al., J. Invest. Derm. 99:830-835, 1992, for reasons of record in the previous Office Action. Note that claims 80-82 have been amended to depend from claim 149. Note further that Paludan specifically teaches assaying for IL-8 mRNA, consistent with those claims. With

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respect to claims 159-160 which recite that the skin has been contacted with an external agent that causes dermatitis, Paludan et al. teach their method for assaying cytokines that have been shown to be present in “epidermis of allergic patch-test reactions, and allergic contact dermatitis”, such that the person of ordinary skill in the art would immediately recognize that they were suggesting the use of the assay following exposure to agents that cause dermatitis.

Applicants argument of this rejection with respect to the “low percentage of positive results” has been fully addressed above. Perfection is not required here, merely the ability to detect the desired nucleic acid with a *reasonable* expectation of results. It is noted that the claims do not require any particular method of isolation nor success rate, nor does the disclosure teach that there is anything special about the method used.

Applicants argue that the Paludan reference teaches that the amount of mRNA recovered was too small for measurement. This argument has been fully considered but is not deemed persuasive because the ability to measure the RNA was not shown to affect the expectation of success. As is well known in the art, the advantage of PCR is that it allows amplification of minute, even undetectable quantities of nucleic acids. Nowhere does Paludan state that amplification was not achieved on samples with amounts of RNA too small to detect. In fact, at page 834, Paludan states that “The total RNA yield from small skin samples is frequently below measurement, and therefore we related the signal obtained with IL-8 primers to that obtained with primers for GAPDH cDNA.” Clearly Paludan did not consider small, even unmeasurably so, samples to be an impediment to success. Applicants argument that Paludan’s use of scraping equates to a teaching against tape stripping has been fully considered but is not deemed persuasive. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicants have failed to make the case that one of ordinary skill in the art would not have been motivated to modify Garofano’s method to include analysis of RNA as taught by Paludan et al.

The Krueger declaration has been addressed above.

Applicants arguments that the lack of published reports of the claimed invention are probative of non-obviousness are not persuasive. One cannot conjecture as to why other groups

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have not pursued this line of experimentation, nor can one draw conclusions as to non-obviousness nor lack of expectation of success based upon the absence of publication.

Claim 155 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Garofano et al., Adv. Forensic Haemogenet 6:281-283, 1996, in view Paludan et al., J. Invest. Derm. 99:830-835, 1992, , Ramsay et al., U.S. Patent Number 6,056,859 and Furcht et al., U.S. Patent Number 6,054,277, for reasons previously of record.

Applicants traversal of this rejection has been answered above with respect to Garofano and Paludan. Applicants arguments of the two patents have been fully considered but are not deemed persuasive because applicants are arguing the references in a piecemeal analysis, rather than in the combination in which they were cited. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Claim 87 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Garofano et al., Adv. Forensic Haemogenet 6:281-283, 1996, in view of Frayne, U.S. Patent Number 5,811,239, for reasons previously of record.

Applicants traversal of this rejection has been answered above with respect to Garofano and Paludan. Applicants arguments of the Frayne patent have been fully considered but are not deemed persuasive because applicants are arguing the references in a piecemeal analysis, rather than in the combination in which they were cited. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

No claim is allowed.

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M. *Effective 1/21/2004, Dr. Spector's telephone number will be 571-272-0893.*

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623. *Effective 1/21/2004, Dr. Kunz' telephone number will be 571-272-0887.*

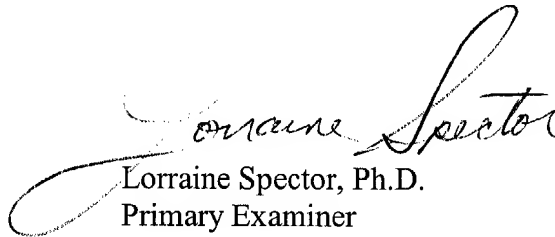
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original

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signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228. *Effective 1/21/2004, Dr. Spector's fax number will be 571-273-0893.*



Lorraine Spector, Ph.D.
Primary Examiner

12/15/2003